

Anthrax Vaccine Immunization Program

Health-Care
Provider's
Briefing



14 January

Key Messages

- **Your health & safety are our #1 concerns**
- **Anthrax vaccine is safe and effective**
- **The threat of anthrax is deadly and real**
- **Vaccination offers a layer of protection, in addition to antibiotics and other measures, needed for certain members of the Armed Forces**

History of AVIP

- **Secretary of Defense ordered the AVIP in Dec 97**
- **Vaccinations began in Southwest Asia in Mar 98**
- **Vaccinations began in Korea in Aug 98**
- **Vaccine shortage caused slowdowns in 2000-2001**
- **AVIP resumed in 2002, after supply of FDA-licensed anthrax vaccine restored**
- **Injunction imposed, then lifted:**
 - **Federal Judge ordered injunction 22 Dec 03**
 - **FDA ruled anthrax vaccine effective regardless of route of exposure on 30 Dec 03**
 - **Judge lifted injunction on 7 Jan 04; DoD resumed AVIP**

Status of AVIP

- **Status:**
 - **FDA ruled anthrax vaccine is safe and effective regardless of route of anthrax exposure**
 - **Mar 98 to Jan 04: Over 3.7 million doses to over 1 million people**
 - **18 human safety studies**
 - **7 reviews by independent panels of civilian physicians, each affirming safety and effectiveness of the vaccine**

Independent Scientific Reviews

- **Food & Drug Administration (*Federal Register* 2004; 69: 255-67)**
- **Armed Forces Epidemiological Board (AFEB), advising DoD, 1994 to present**
- **Cochrane Collaboration, Oxford, *Vaccine* 1998; 16: 880-884**
- **Working Group on Civilian Biodefense, *JAMA* 1999; 281: 1735-1745**
- **CDC's Advisory Committee on Immunization Practices (ACIP) (*MMWR* 2000; 49 (RR-15): 1-20)**
- **Anthrax Vaccine Expert Committee (AVEC), 1998**

to
14 January

AVIP Lessons Learned

- **We must ensure a continuous supply of vaccine**
- **We must educate all stakeholders early: patients, family members, health-care professionals, general public**
- **Our patients perceive the risk-benefit ratio from BW vaccines differently than other “routine” vaccines**
- **A strong foundation of research-based, third-party endorsed, published science is critical to credibility**
- **Health care provider involvement is the key to success**

Background: Anthrax Infections

- **Recognized as an illness for centuries**
- **Spores can survive in soil for decades**
- **Once common where livestock were raised**
- **Animal anthrax controlled using vaccine for livestock**
- **Human infection may result from direct contact with infected animals or animal products or anthrax spores**

Anthrax

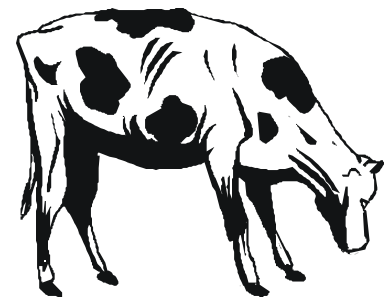
- **Anthrax can be loaded into shells, missiles, bombs, and other weapons.**
- **Inhalational anthrax is highly lethal.**
- **Vaccination is critical for your protection.**
- **This vaccination program is required, except for legitimate medical exemptions.**
- **Anthrax vaccine is safe and effective, according to FDA, CDC, and National**

Threat

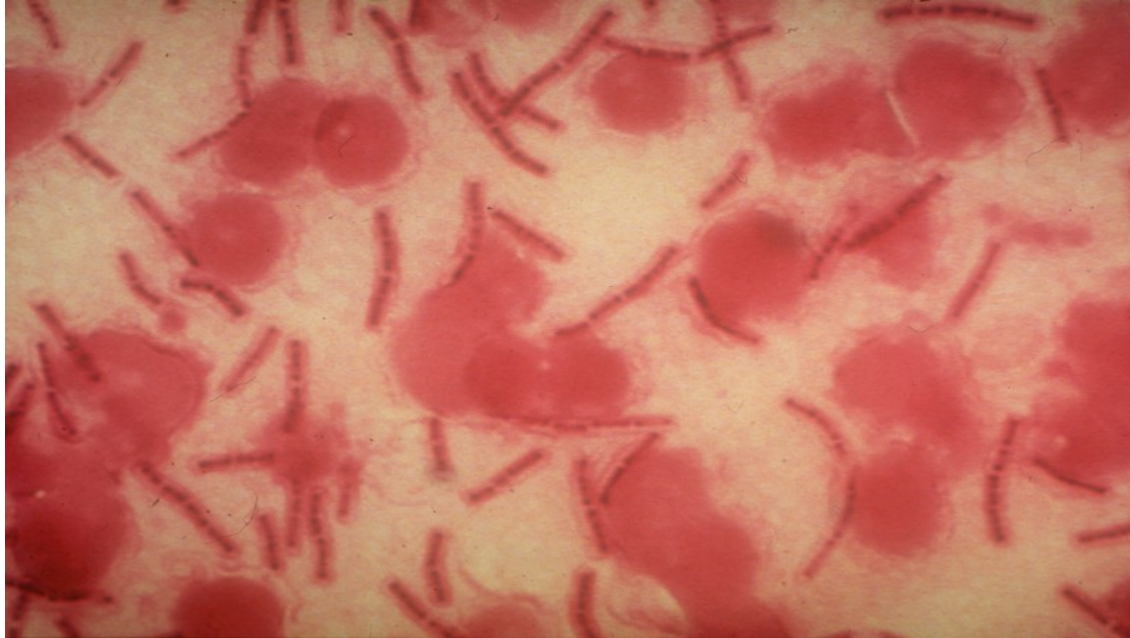
- **Anthrax: the most likely Bio-Warfare agent:**
 - **Relatively easy and cheap to produce**
 - **Can be stored for a long time**
 - **Can be dispersed in air in a variety of ways**
 - **Odorless, colorless, tasteless, difficult to detect**
 - **Inhalational anthrax is highly lethal**
- **Anthrax can cause widespread illness and death among unprotected people.**

Epidemiology of Anthrax

- **Disease of herbivores**
- **Humans infected via animal products**
- **Dramatic reduction in U.S. since early 1900s**
- **Still a problem in Asia and Africa**
- **Terror attacks via U.S. mail in Fall 2001**



Microbiology of Anthrax



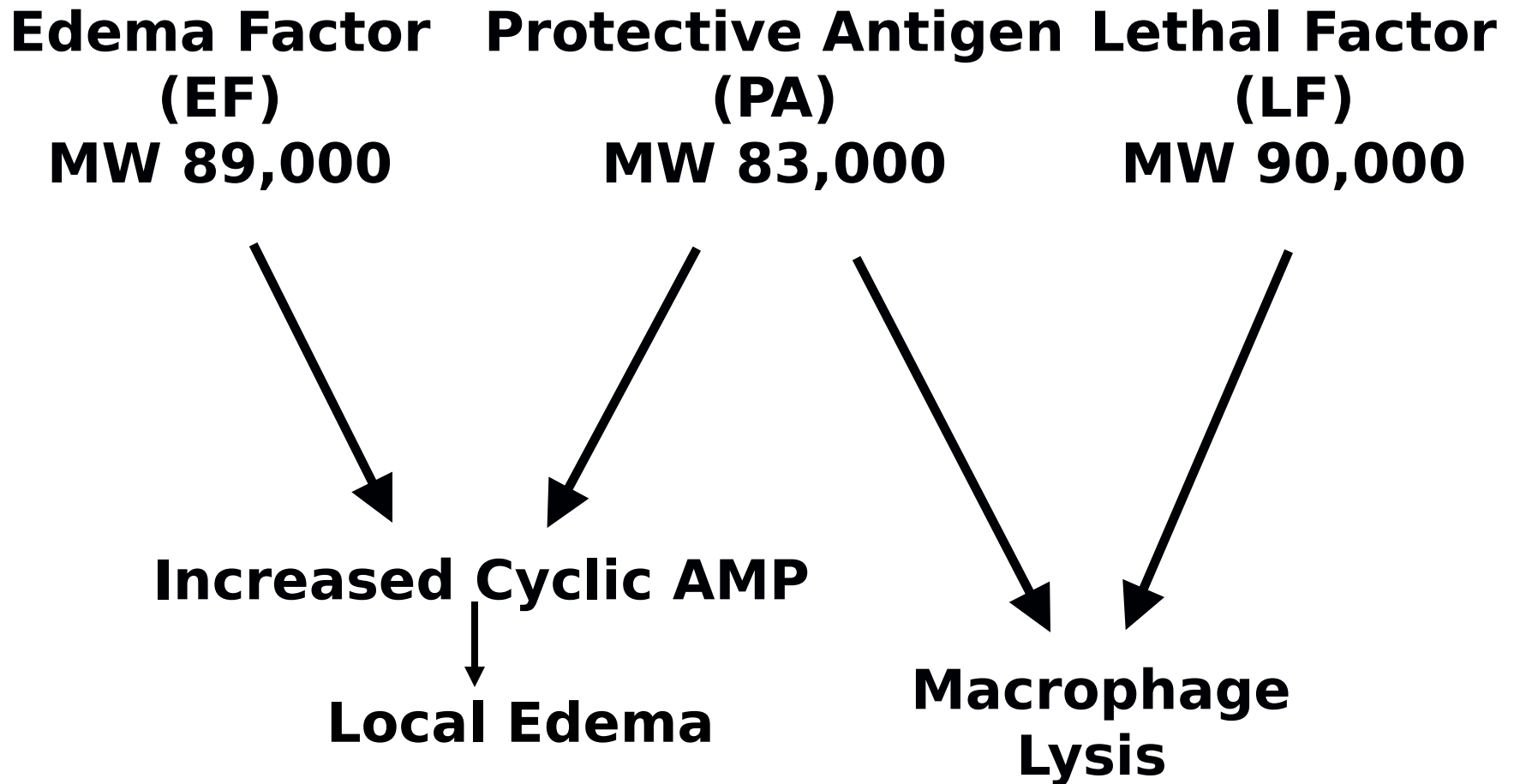
Gram-positive spore-forming rod

Pathogenesis

- **Spore enters skin, GI tract or lung**
- **Ingested by macrophages**
- **Transported to regional lymph nodes**
- **Germinate in regional nodes, mediastinum (inhalational)**
- **Local production of toxins**
- **Edema & necrosis**
- **Bacteremia & toxemia**
- **Seeding of other organ systems**

Anthrax Toxin

Production & Effects



Cutaneous Anthrax

- **Greater than 95% of naturally occurring cases**
- **Spores enter breaks in skin after contact with contaminated animal products**
- **Within a few days, bump (papule) turns into blister (vesicle), then ulcer with black area in center (eschar)**
- **5% to 20% case-fatality rate if untreated**
- **Mortality with treatment < 1%**



Gastrointestinal Anthrax



- **Ingestion of insufficiently cooked meat from infected animals**
- **Symptoms include nausea, vomiting, fever and severe abdominal pain**
- **Lethality rate is 50% despite treatment**

Inhalational Anthrax

- **Inhalational anthrax occurs when spores enter the body through the lungs**
- **Not transmitted person to person**
- **Spores migrate to lymph nodes where bacteria multiply and produce lethal toxins**
- **Toxins cause bleeding and destruction of the brain or vital organs in the chest, resulting in death**

Diagnosis of Inhalational Anthrax

- **Initial symptoms nonspecific**
- **Development of respiratory distress**
 - **Chest X-ray with widened mediastinum**
 - **Usually no infiltrates**
- **Sputum not helpful**
- **Nasal swabs not individually meaningful**
(www.bt.cdc.gov/DocumentsApp/faqanthrax.asp#Q500)
- **Blood cultures - positive late in course of illness**
- **Hemorrhagic pleural effusion or meningitis**

Chest X-Ray of Inhalational Anthrax



Inhalational Anthrax Treatment

- **Early IV antibiotics and intensive care required**
 - **Mortality may still reach 50%**
 - **Penicillin - historical treatment**
- **Current treatment of choice:**
 - **Ciprofloxacin 400 mg IV q 8-12 h**
 - **Doxycycline 200 mg IV x 1,
then 100 mg IV q 12 h**
- **Disease not spread by respiratory secretions**
 - **Use 'Standard Precautions'**

Post-Exposure Prophylaxis

- **Starting antibiotics within 24 hours after aerosol exposure should provide significant protection**
 - **Ciprofloxacin 500 mg po BID**
 - **Doxycycline 100 mg po BID**
- **Most effective when combined with vaccination**
- **Antibiotics are still indicated even when fully immunized, to achieve survival as close to 100% as possible**

Anthrax Vaccine Facts

- **Vaccine primes body's natural defense system to fight anthrax**
- **Anthrax vaccine cannot cause anthrax**
- **Licensed by the FDA since 1970**
 - **Safely administered in the U.S. to at-risk veterinarians, laboratory workers, and livestock handlers**
 - **Over 3.7 million doses to over 1 million personnel between Mar 98 and Jan 04**
- **Manufactured in U.S. by BioPort Corporation**
 - **Lansing, Michigan**

Vaccine Quality Control

- **Each lot of each vaccine manufactured in the U.S. must meet FDA specifications and prescribed standards per 21 CFR 610, before release into interstate commerce**
 - **Potency, Sterility, Purity, General Safety**
- **Testing on each lot done by manufacturer; results submitted to and audited by the FDA**

Handling Anthrax Vaccine

- **Vaccine must be refrigerated**
 - **Store and maintain between 36 and 46 degrees Fahrenheit (2 - 8° C)**
- **DO NOT FREEZE**
- **Once vial opened, use until expired**
 - **Discard if contaminated**
- **Go to USAMMA web site for guidance on vaccine temperature, storage and handling:**
 - <http://www.usamma.army.mil/anthrax/antxhome.htm>

Vaccine Efficacy in Humans

- Brachman et al. *Am J Public Health* 1962;52:432-45
 - **Efficacy: 92.5% (95% CI: 65-100%), jointly against cutaneous and inhalational anthrax**
 - **Inhalational anthrax:**
 - **5 cases / 448 unvaccinated people**
 - **0 cases / 149 vaccinated people**
 - **Manufacturing improvements, 1960s CDC study**
 - **Microaerophilic, more PA, less EF and LF**
 - **Safety and efficacy reaffirmed by FDA advisory panel, Federal Register 1985; 50:51002-117**
 - **Final Rule by FDA 30 Dec 03; published in *Federal Register* on 5 Jan 04, vol 69: pages 255-67**

Inhalational Anthrax: Vaccine Efficacy in Non-Human Primates

- **55 monkeys vaccinated twice**
 - **Challenged with spore aerosol of dozens to thousands of times the median lethal dose, 8, 16, 38, or 100 weeks later**
 - **52 survived**
- **10 monkeys vaccinated once**
 - **Challenged with aerosol 6 weeks later**
 - **All survived**
- **Overall, 62 of 65 survived, 95% vaccine protective efficacy against inhaled anthrax spore challenge**

Response to Vaccination

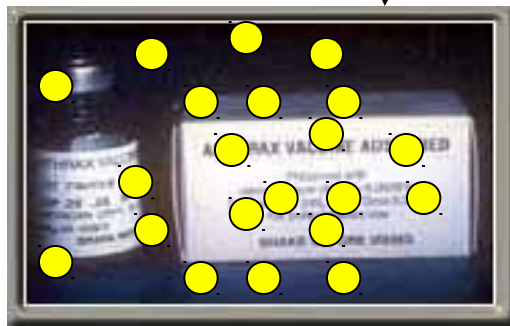
- **Anthrax vaccine, like other vaccines, stimulates your body to produce protective antibodies**
- **Each dose of vaccine adds to protection, like walking up a set of stairs**
- **The full series is needed to obtain maximum and on-going protection.**

How Anthrax Vaccine Prevents Disease

Anthrax Bacteria

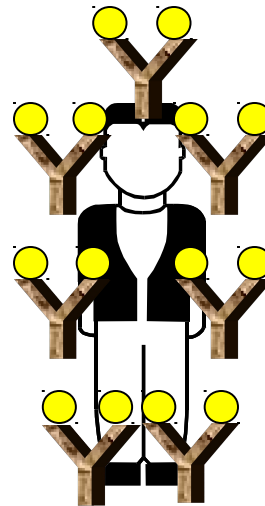
Protective Antigen (PA)

filtered



Vaccine contains PA, extracted from weakened nonlethal anthrax bacteria.

Disease



Immune system develops antibodies (Y) to PA, protection from disease.

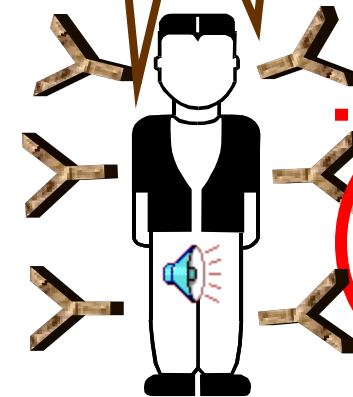


Exposure

Lethal Factor



Edema Factor



Antibodies "neutralize" PA, common part of anthrax toxins.

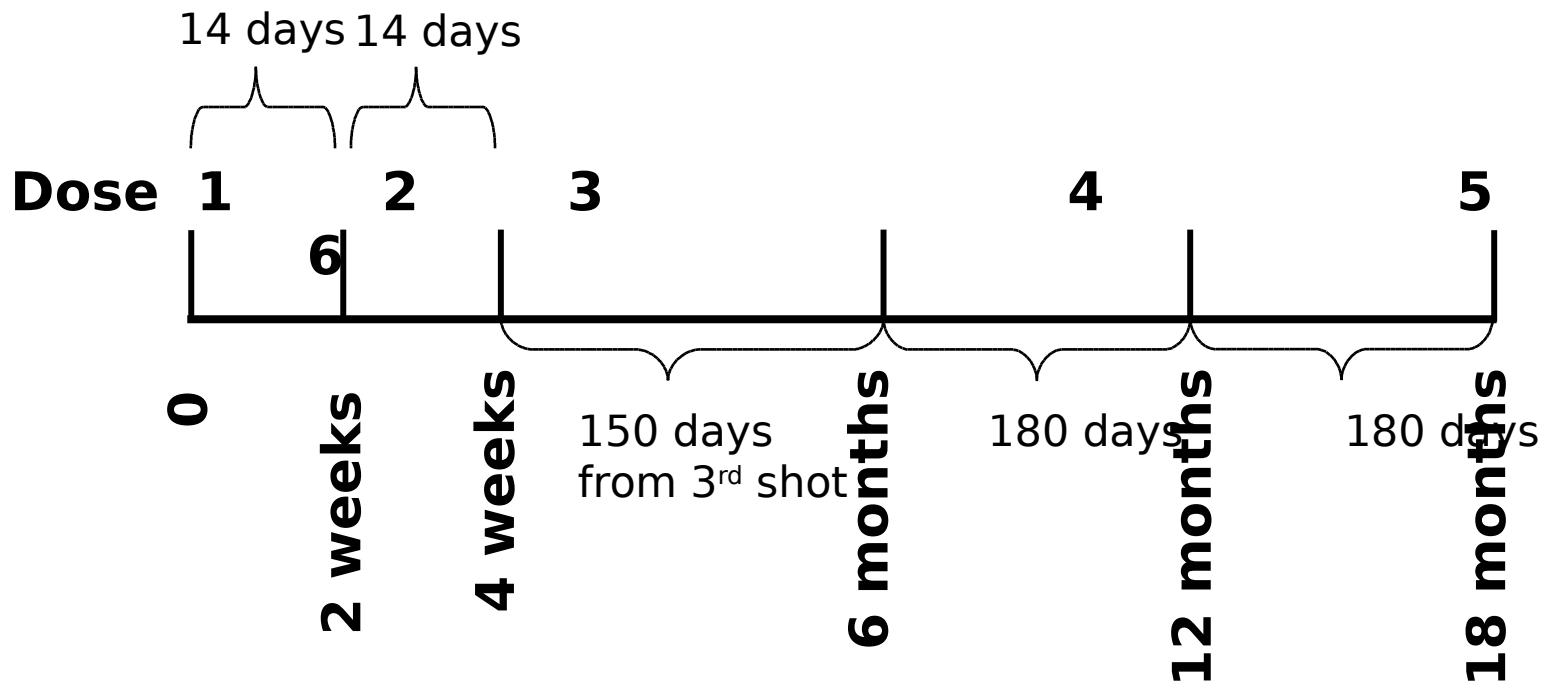


Disease & Death

Vaccine Protection Against Different Strains

- **Vaccine efficacy demonstrated against numerous anthrax strains (types) in various animal studies**
- **Protective antigen (PA) is the common disease-causing protein in all anthrax strains**
- **Blocking PA blocks the disease**
- **National Academy of Sciences: Anthrax vaccine is “an effective vaccine for the protection of humans against anthrax, including inhalational anthrax, caused by all known or plausible engineered strains”**

Vaccine Schedule

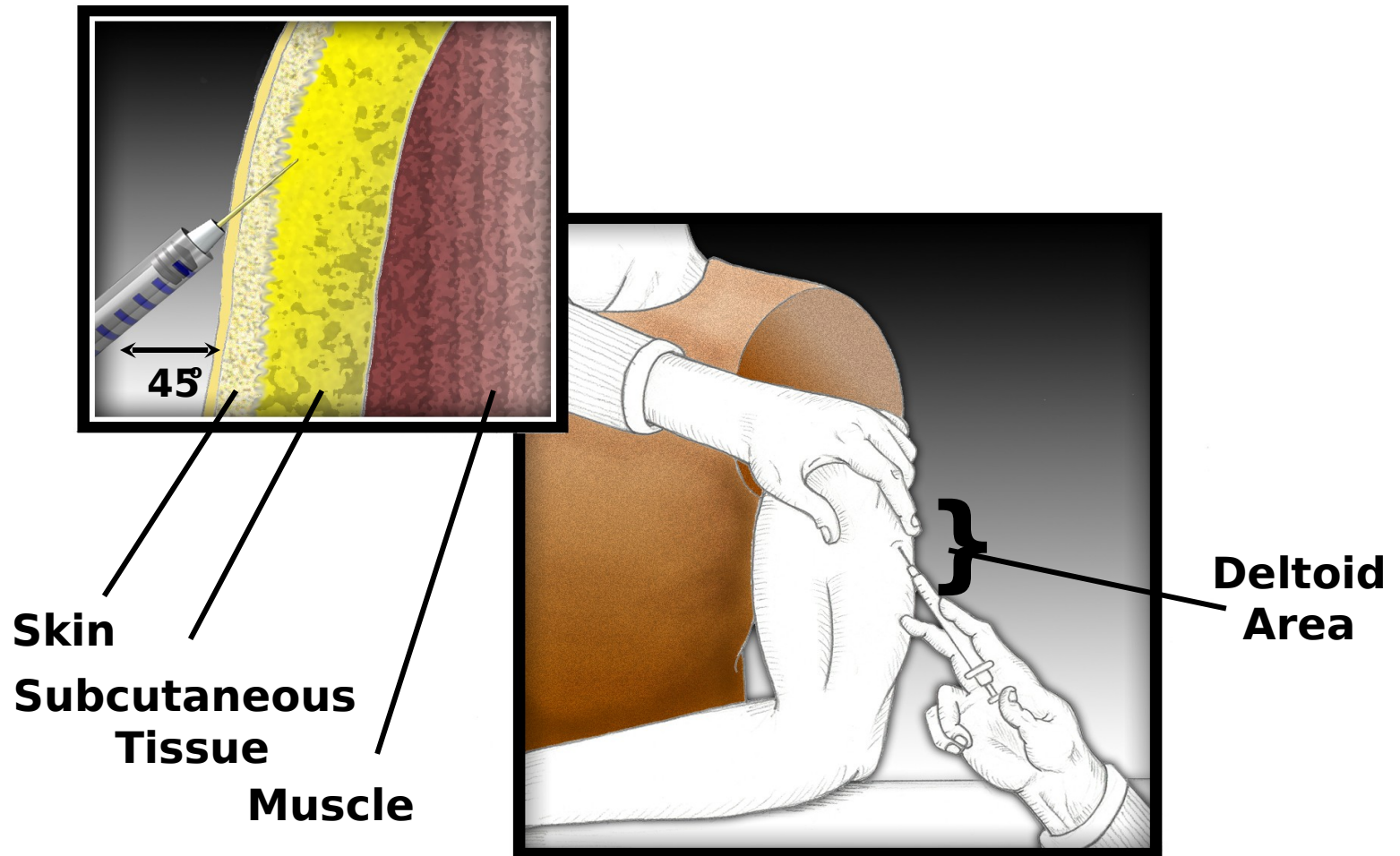


- **Six shots over 18 months, plus annual boosters**
- **Do not compress the schedule**
- **Adjust schedule for individual delays**

Anthrax Vaccination Schedule

- **DoD policy is to adhere to FDA-licensed vaccination schedule.**
- **Do NOT compress dosing schedule.**
- **Give late doses ASAP - adjust timing of later doses according to standard schedule.**
- **Use clinical judgment when managing individual cases.**
- **Seek subspecialty consultation as warranted.**

Vaccination



Pregnancy

- **Vaccinations routinely deferred during pregnancy**
- **Before vaccination, ask each woman if menses normal and on time. Postpone, if pregnancy possible.**
- **No reason to delay conception after vaccination:**
 - **Anthrax-vaccinated & unvaccinated women at Fort Stewart (JAMA, 2002):**
 - **same rates of conception**
 - **same rates of delivery**
- **Vaccination during pregnancy: Rates of birth defects under study. Rates before & after pregnancy are same as for unvaccinated women.**
- **Encourage pregnancy testing.**
- **Details at www.anthrax.mil**

Contraindications

- **Hypersensitivity reaction to a previous dose of anthrax vaccine or vaccine component**
- **Younger than 18 or older than 65 (pending further study)**
- **HIV positive**
- **Temporary deferral**
 - **Pregnancy, suspected pregnancy**
 - **Active infection/illness with fever**
 - **Depressed immune response, including corticosteroid or other immunosuppressive treatment**

Injection-Site Reactions After Anthrax Vaccination

- For both genders, most injection-site reactions last 1 to 3 days and go away on their own
- From Hawaii, Korea, Ft. Bragg, Ft. Detrick, 1993-

2000: Redness, itching, swelling (lasting a few days)

- **Less than 1 inch: men up to 30%, women up to 60%**
- **1 to 5 inches: 1% to 5%**
- **Greater than 5 inches: 1%**
- **Swelling may extend below elbow**

- **Soreness or local pain in 8% to 19%**

Systemic Events (Events Away from Injection Site)

- **From 5% to 35% will notice:**
 - **Muscle aches, joint aches, chills, low-grade fever,
no appetite, headaches, nausea, malaise, related
symptoms**
 - **Women experience these symptoms more often
than men**
 - **These symptoms usually go away in a few
days,
less than a week**

Injection-Site Reactions and Systemic Events

- **Screen for previous adverse reactions**
- **Treat and pre-treat adverse events**

See clinical guidelines at www.vhcinfo.org

- **Do not give next dose if side effects persist from previous vaccination**
- **Issue temporary exemption if symptoms persist**
- **Consult provider skilled in diagnosis and management of vaccine adverse events for permanent exemption**

Long-Term Studies

- **Anthrax-Vaccine Recipients Followed for Years**
 - **TAMC-600 Survey (Tripler Army Medical Center)**
 - **Defense Medical Surveillance System (inpatient and outpatient visit surveillance)**
 - **Naval Health Research Center (inpatient and outpatient visit surveillance)**
- **Anthrax-Vaccine Recipients Followed for Decades**
 - **Fort Detrick Multi-Dose, Multi-Vaccine Safety Studies (1940s to 1970s)**
 - **Fort Detrick Special Immunization Program**

Adverse Event Reporting

- **Vaccine Adverse Event Reporting System (VAERS)**
 - **FDA reviews 100% of adverse-event reports submitted to either FDA or DoD**
 - **Reviewed by independent panel of civilian physicians for 4 years**
 - **Anyone can submit a VAERS Form**
- **DoD requires a VAERS Form submission for:**
 - **Loss of duty 24 hours or longer ($\geq$ 1 duty day)**
 - **Hospitalization**
 - **Suspected vaccine vial contamination**
- **Other submissions encouraged**
- **VAERS Form may be obtained from:**
 - **Your clinic, 1-800-822-7967, or www.vaers.org**

Reserve Component Adverse-Event Guidance

- **Someone with an adverse event in a non-duty status possibly associated to any vaccination:**
 - **Seek medical evaluation at a DoD, USCG, or civilian medical treatment facility, if necessary**
 - **Must report the event to your unit commander or designated representative as soon as possible**
 - **See local medical department or squadron for guidance**
- **Commander will determine Line of Duty and/or Notice of Eligibility status, if required**

Access to DoD Military Treatment Facility (MTF)

- **Once designated to receive anthrax vaccine, the following personnel may receive any dose at any MTF:**
 - **Active component**
 - **Reserve component (Must be in a duty status)**
 - **Emergency essential DoD civilian and contract personnel**
 - **U.S. Coast Guard as applicable**
- **Mass immunizations require prior coordination with MTF.**

Record Keeping

- **Automated immunization tracking**
 - **Service systems and DEERS central repository**
- **Written entries:**
 - **Health record**
 - **Adult Preventive and Chronic Care Flowsheet (DD form 2766 or DD form 2766C)**
 - **Yellow Shot Card (PHS-731)**
- **Required documentation:**
 - **Date immunized, name of vaccine, manufacturer, lot number, series number, dosage, provider name and MTF address**

What Troops Deserve From Their Health-Care Providers

- **Care, concern, and support**
 - **Q&A page at www.anthrax.mil explains many things of interest to your patients**
- **Quality health care, quality vaccine delivery**
- **Effective solutions to health-care needs**
- **Open communication and advice**
- **Compassion in dealing with adverse events**
- **Assistance in reporting adverse events**

Conclusions

- **Anthrax is a lethal threat to our forces.**
- **The anthrax vaccine is safe and effective.**
- **Personal protective measures are important**
- **The life-saving benefits of anthrax vaccine make this an essential immunization program.**
- **Health-care providers are key to Service Member understanding of the value of anthrax vaccination**

For Program or General Scientific Information:

- Chain of Command
- AVIP Agency
 - Website: www.anthrax.mil
 - Customized answers to your individual questions via E-Mail: vaccines@amedd.army.mil
 - Toll-Free: [877.GETVACC](tel:877.GETVACC)
- CDC National Immunization Hotline: [800.232.2522](tel:800.232.2522)
- www.bt.cdc.gov
- www.aviationmedicine.com

For Medical Information:

If a Reserve Component or Active Duty member of the Armed Forces presents at your office for a condition they believe may be an adverse event caused by a vaccination, please provide care appropriate to their condition and contact the following as soon as possible for coordination and payment:

- Walter Reed Vaccine Healthcare Center: [202.782.0411](tel:202.782.0411)
(www.vhcinfo.org)

- Information for Civilian Healthcare Providers: Call the Military Treatment Facility (MTF) where the member is enrolled -OR- contact the Military Medical Support Office (MMSO): [888-647-6676](tel:888-647-6676) if the member is